Ovarian Sertoli-Leydig Cell Tumor with High Serum Level of alpha-Fetoprotein

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ABSTRACT

A case of an ovarian Sertoli Leydig cell tumor (SLCT) associated with elevated serum alpha-fetoprotein (AFP) levels occurred in a 16-year-old girl. She had no signs of virilization or defeminization at the operation. In the abdominal cavity, a large and well demarcated tumor had replaced the right ovary. After the surgical removal of the tumor, the serum level of AFP decreased to within the normal limits.

Microscopic examination of the tumor revealed intermediately differentiated SLCT with a retiform component. Immunohistochemical studies demonstrated the immunoreactivity of AFP in Leydig cells and Sertoli cells.

The mechanisms of AFP production by SLCT were discussed here along with a review of the literature.

Key words: AFP, Sertoli-Leydig cells, Ovarian tumor

INTRODUCTION

SLCT is a rare ovarian neoplasm representing 0.6% of all malignant ovarian tumors. Approximately 54% of SLCT cases show functional virilization. AFP, a representative marker of liver cell carcinoma and germ cell tumors, is an infrequent finding in association with sex cord-stromal tumors, as is SLCT (1, 2).

In the English medical literature, there have been 15 cases of SLCT with AFP since Benefield *et al* reported the first case (3, 4, 5). There has also been some discussion of the origin of AFP producing cells.

In this report, we present an additional case in which a patient with an ovarian SLCT had a high serum level of AFP that was secreted from Leydig cells and/or Sertoli cells.

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REPORT OF CACE

A 16-year-old girl was admitted to the hospital due to abdominal discomfort. Physical examination revealed an isolated right ovarian tumor. She had no signs of amenorrhea or masculization. Laboratory examination demonstrated normal blood cell count, electrolytes, renal function and liver profile. The serum level of AFP was 446 ng/ml, while carcinoembryonic antigen (CEA) and sialyl Lewis X (SLX) were within normal limits. An exploratory laparotomy disclosed a large tumor replacing the right ovary. No evidence of ascites or intra-abdominal metastasis was present. A right salpingo-oophorectomy was performed. Two weeks after the operation, serum lcvel of AFP had decreased to 47 ng/ml (normal range 40 ng/ml).

She was given 3 cycles of standard chemotherapy against ovarian tumor. Four years after surgery, she was still free from disease and AFP was within normal limits.

MATERIALS AND METHODS

Fifteen sections from the tumor were embedded in paraffin and processed for light microscopy in a routine manner. Histologic sections were stained with hematoxylin-eosin (H & E), periodic acid Schiff, Sudan III, silver staining, Grimerius and Fontana-Masson staining. Immunohistochemical study was carried out on the formalin fixed sections with mouse anti-human AFP (Dako, Kyoto, Japan) anti-keratin (Dako, Kyoto, Japan), anti-epidermal membrane antigen (EMA)(Dako, Japan), anti vimentin (Dako, Kyoto, Japan), anti S-100 (Dako, Kyoto, Japan), and anti neuron specific enolase (NSE) (Dako, Kyoto, Japan) monoclonal antibodies using streptavidin-biotin (Histofine, Seikagaku Pharmaceutic Co. Tokyo, Japan).

RESULTS

Gross findings;

This tumor (14x 14x 14 cm) was enclosed by a smooth, elastic, soft, tan-colored capsule. When cut, it revealed multiple cysts surrounded by solid tissue, part of which was creamy. Necrosis and hemorrhage in the tumor were not remarkable (Fig. 1). The contralateral ovary, uterus, both fallopian tubes and abdominal cavity were normal.

Light microscopic findings;

The microscopic features were not uniform. The solid part of the tumor mainly consisted of four different component types. The majority of the tumor cells were small with round to oval nuclei and had scanty cytoplasm, consistent

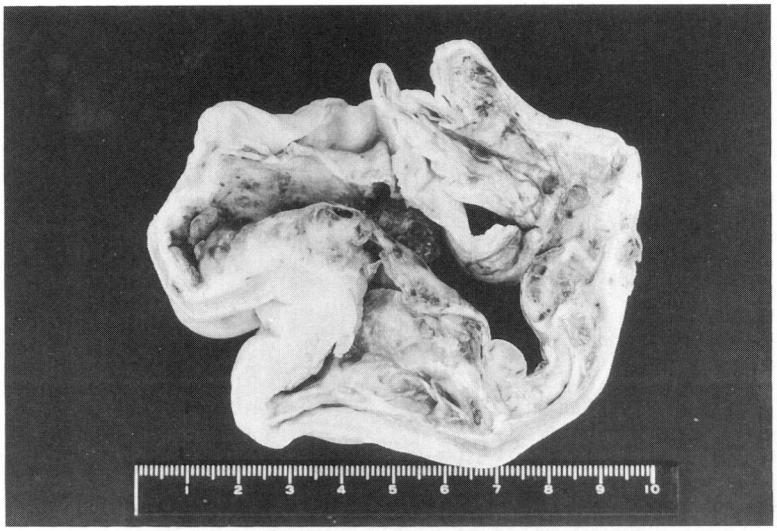

Fig 1. Cut surface of the tumor showed multiple cysts and solid lesions

with immature Sertoli cells. These formed cords, sheets, and variable sized aggregations; they were separated by variable numbers of Leydig cells and indifferent stromal cells (Fig. 2a). Second, there were the well-differentiated tubular microstructures composed of hollow or solid tubules similar to those described in Sertoli cell tumors (Fig. 2b). Lipid was present in the cytoplasm of the cells (not shown). The third component was single cell or nests of cells with abundant eosinophilic cytoplasm and nuclei with prominant central nucleoli which were thought to be Leydig cells. However, no Reinke's crystals were observed

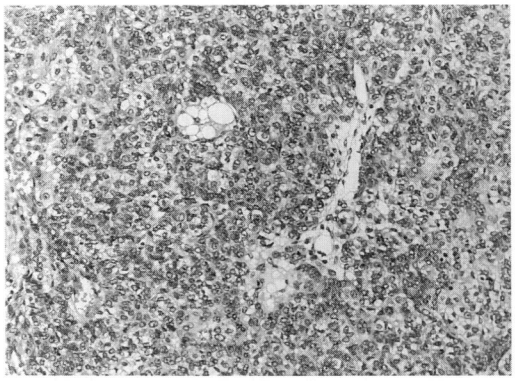

Fig 2a. Trabecular Sertoli cell; typical of intermediate Sertoli cell tumors (x200 H & E)

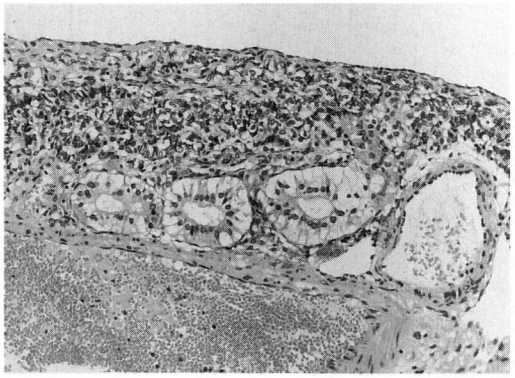

Fig 2b. Typical Sertoli cell tumor area (x200 H & E)

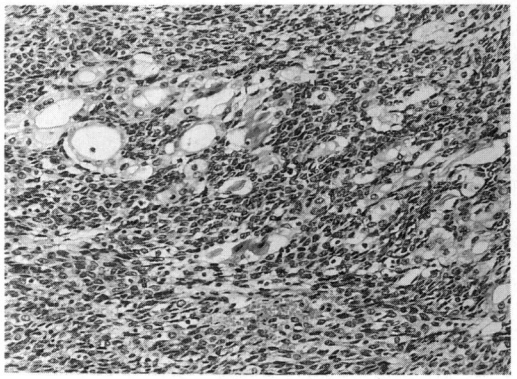

Fig 2c. Leydig cells with abundunt eosinophilic cytoplasm are observed in intermediate SLCT, however, no Reinke's crystals are observed. (x200 H & E)

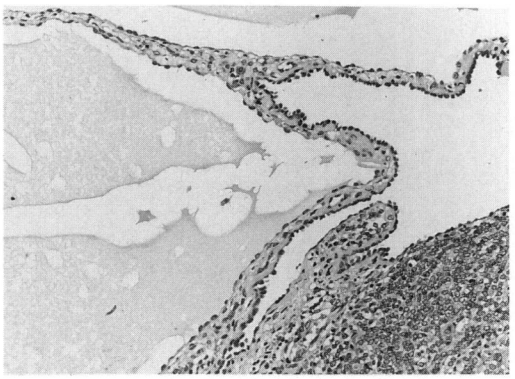

Fig 2d. Retiform (reticular) pattern within the SLCT; these patterns are not major components. (x200 H & E)

(fig. 2c).

Lipid was present in the cytoplasm of the Leydig cells, and AFP was strongly positive in such cells (Fig. 3a). Finally, as a minor component, a retiform pattern was present (Fig. 2d), and AFP was also detected in this part (Fig. 3b).

The immunohistochemical study showed that cytokeratin was positive in the well-differentiated Sertoli cells, and vimentin was expressed in the immature Sertoli cells. Other monoclonal antibodies, S-lOO, EMA and NSE were not reactive to SLCT (data not shown).

DISCUSSON

AFP is a well known marker of hepatocellular carcinoma and gonadal and extra-gonadal endodermal sinus tumor (6). It has occasionally been described in

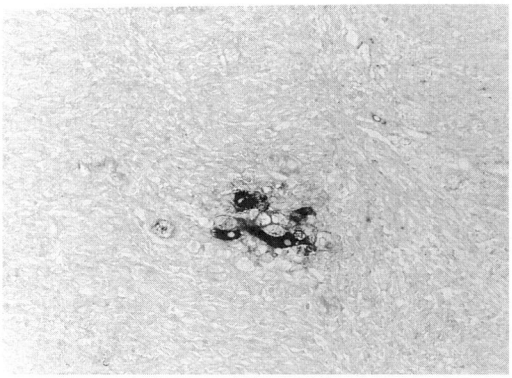

Fig 3a. AFP was positive in the Leydig cell (x200, counter staining ; hematoxylin)

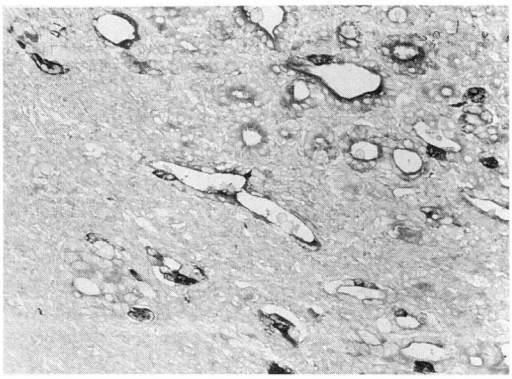

Fig 3b. AFP was detected in reticular pattern (x200, counter staining ; hematoxylin)

other types of gonadal neoplasms, in carcinoma of ovarian epithelium and rarely, in granulosa cell tumor and mixed mesodermal tumor (7).

The present case was classified as an intermediately differentiated SLCT. AFP was detected in the Leydig cells and well differentiated Sertoli cells by an immunohistochemical study. Futhermore, the serum level of AFP rapidly decreased after surgical removal. These facts justified the conclusion that our case was one where AFP was produced by SLCT.

Fifteen cases of AFP resulting in SLCT have been reported in the literature since Benfield *et al* first reported a similar case in 1982 (8).

In the literature, AFP is reported to localize in Leydig cells, Sertoli cells, hepatoid cells or undifferentiated cells, according to immunohistochemical data. However, the nature of AFP producing cells in SLCT is still debated (9).

The mechanism of AFP production by Leydig cells in sex cord stromal tumor is unknown. It might be due to AFP gene derepression related to oncogenesis during tumor development (10, 11) ; other researchers have attributed it to neometaplasia, which is the term for the occurrence of heterologous elements in SLCT. A few cases of SLCT have shown heterologous elements in endodermal components, including the gastrointestinal epithelium. AFP might be produced by such a functional neometaplasia in an endodermal component, i.e. gastrointestinal epithelium or hepatoid differentiation (12, 13).
Examination of this case did not reveal enough evidence to provide a conclusive answer to that question.

We hereby add the 16th report on rare tumors of so-called "AFP producing SLCT ".

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